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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/802,585	03/17/2004	Le Huang		3879

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EXAMINER	
RAO, DEEPAK R	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 09/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/802,585	HUANG, LE	
	Examiner	Art Unit	
	Deepak Rao	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) *2,3,5,6,9,10,12,19,20,22,29 and 30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,7,8,11,13-18,21,23-28 and 31-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20040317*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-33 are pending in this application.

Election/Restrictions

Applicant's election **without** traverse of the inventions of Groups III, VI and IX (drawn to claims 1, 4, 7, 8, 11, 13-17, 18, 21, 23-27, 28 and 30-33, in the reply filed on July 3, 2006 is acknowledged.

In the previous office action, election of a single invention was required and in response applicant elected inventions of three groups. As all three groups of inventions are drawn to the same product (anhydrous amorphous form of fluvastatin sodium), upon reconsideration, the inventions of Groups VI and IX are combined with Group III and examined together. Applicant is thereby notified that the restriction between Groups III, VI and IX is withdrawn.

Claims 2-3, 5-6, 9-10, 12, 19-20, 22 and 29-30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on July 3, 2006. As applicant's election is without traverse, it is suggested that the withdrawn claims be canceled.

Specification

This application contains 6 drawings (sheets 1-3 showing Formula I-III and sheets 4-6 showing Figures 1-3). Each of the graphic forms appearing in the drawings should be labeled as a separate figure, see 37 CFR § 1.184. The Brief Description of the Drawings in pages 5-6 is with respect to Figures 1-3 and **no** description is provided with respect to the first three sheets of

drawings containing formula I-III. As the formulae depicted in sheets 1-3 are already present in the specification at pages 1-2, the content of drawing sheets 1-3 is repetitive and redundant. Appropriate correction of the drawings or the brief description is required as set forth in 37 CFR § 1.74 and § 1.84. "When there are drawings, there shall be a brief description of the several views of the drawings and the detailed description of the invention shall refer to the different views by specifying the numbers of the figures, and to the different parts by use of reference letters or numerals (preferably the latter)".See MPEP § 608.01(f).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 33 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use of anhydrous amorphous form of fluvastatin sodium as a medicament for treating hyperlipidemia, hypercholesterolemia or atherosclerosis, does not reasonably provide enablement for the use of the compound in **preventing or ameliorating** the recited diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art,

4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed. The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations.

The instant claim recites the use of the compound not only for treating but also for "preventing or ameliorating" and the specification fails to enable one skilled in the art for the recited use. It is inconceivable as to how the claimed compounds can treat the extremely difficult diseases embraced by the instant claims. The diseases listed in the claim are:

- Atherosclerosis. The gradual build-up of cholesterol-rich plaque on the inner wall of a large artery, which causes them to narrow and harden. Atherosclerosis is a leading cause and indicator of potential coronary artery disease.
- Hyperlipidemia. High blood levels of cholesterol and triglycerides.
- Hypercholesterolemia. The presence of high levels of cholesterol in blood.

The specification does not provide any guidance regarding how to identify the subject 'in need of the claimed method of 'preventing or ameliorating'. There is nothing in the disclosure regarding how this data correlates to the 'preventing or ameliorating' of the various disorders of the instant claims. The disclosure is insufficient such that one skilled art cannot reasonably extrapolate the activity of the compounds to claimed use. The area of receptor interactions is highly structure specific and unpredictable.

Regarding hypercholesterolemia, Vega et al. (PubMed Abstract enclosed) state that "Hypercholesterolemia is a well-established risk factor for coronary heart disease. However, the mechanisms underlying hypercholesterolemia, elevated low density lipoprotein (LDL) in

particular, are not well understood".

Further, there is no disclosure regarding how 'the subject in need of' the **prevention** is identified and further, how types of atherosclerosis, hyperlipidemia and hypercholesterolemia are prevented. In order to determine if any particular claimed compound to be useful in treating, preventing or ameliorating of a disease, first the compound needs to be synthesized, formulated into a suitable dosage form, and subjected to clinical trials with a number of fundamentally different diseases listed above or test the compounds in an assay known to be correlated to clinical efficacy of such treatment. This is a large degree of experimentation.

The direction concerning treating diseases found in the specification merely states applicant's intention to do so. Applicant describes formulation having a recommended dosage amount in the range of 0.5 to 50 mg daily (see page 13), however, since no therapeutic agent having the ability to inhibit HMG CoA reductase has ever been used in the **prevention** of the diseases recited in the claim, one skilled in the art would not find sufficient guidance regarding the dosage regimen required for each of these different diseases. The specification provides one test procedure with no correlation to the assorted diseases covered by the instant claim. Applicant neither asserted nor it is art-recognized that the only procedure provided in the specification is correlated to the clinical efficacy of all of the diseases instantly claimed.

Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24

(CCPA 1970).

'To prevent' actually means *to anticipate* or *counter in advance, to keep from happening etc.* (as per Websters II Dictionary); 'to ameliorate' means *to improve, to revolutionize, to restore*, etc. and therefore it is not understood how one skilled in the art can reasonably establish the basis and the type of subject to which the instant compounds can be administered in order to have the recited effect of **preventing** or **ameliorating**.

MPEP § 2164.01(a) states that "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)". That conclusion is clearly justified here and undue experimentation will be required to practice the claimed invention.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the use of the invention. In view of the breadth of the claim, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4, 7, 11, 13-18, 21, 23-28 and 31-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

1. Claims 1, 4 and 7 recite "**Novel** anhydrous amorphous form..." wherein the term 'novel' is not appropriate claim language.
2. Claim 27 depends from 'any of claims 18-26' which includes the 'withdrawn' claims 19, 20 and 22. Appropriate correction is required.
3. Claim 33 provides for the use of the compound, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 101

Claim 33 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4, 7, 18, 21, 23-27, 28 and 31-33 are rejected under 35 U.S.C. 102(b) as anticipated by Horvath, U.S. Patent No. 6,124,340.

The reference teaches Fluvastatin sodium compound, including the anhydrous amorphous form thereof. See the structural formula in col. 1 and the disclosure regarding form A of fluvastatin sodium in col. 2. The reference teaches that the compound is useful as a pharmaceutical agent, particularly in the treatment of hypercholesterolemia, atherosclerosis, etc. see col. 1.

Claim 4 recites that the 'anhydrous amorphous form of fluvastatin sodium is characterized by an X-ray diffraction pattern substantially in accordance with Figure 3'. The reference discloses fluvastatin sodium salt and further discloses that the lyophilization product comprises of the amorphous form. The X-ray diffraction is an inherent characteristic of the reference disclosed amorphous form as well. It is well settled that PTO can require an applicant to establish that a prior art product does not necessarily possess the characteristics of the claimed product when the prior art and claimed products are identical or substantially identical. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433-434 (CCPA 1977).

Claims 18, 21 and 24-27 are drawn to a process of preparation of the anhydrous amorphous form by dissolving in acetonitrile or alkanol. The reference teaches an analogous process of dissolving fluvastatin sodium in a solvent such as methanol or ethanol for the preparation of the non-crystalline (or amorphous) fluvastatin sodium which is used as the starting

material in a crystallization process, see col. 3-4. The reference also teaches the equivalency of the solvents ethanol, acetonitrile, etc., see col. 4.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 4, 7, 11, 13-18, 21, 23-28 and 31-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Horvath U.S. Patent No. 6,124,340 in view of Kumar et al., WO 00/71116.

Horvath teaches anhydrous amorphous form of fluvastatin sodium, see the disclosure in col. 1-2 regarding the compound and the amorphous form thereof. The reference further teaches that the starting material for the crystallization process is prepared by dissolving in a polar

organic solvent, e.g., methanol or ethanol, see col. 3-4. Claims 1, 4, 7, 18, 21, 23-27, 28 and 31-33 are anticipated by the reference as rejected under 35 U.S.C. 102(b) above.

Claims 8, 11 and 13-17 differ from the reference by reciting a process for the preparation of the anhydrous amorphous form of fluvastatin sodium using a non-hydroxylic solvent and a non-polar hydrocarbon anti-solvent.

Kumar et al. (WO'116) in the analogous art, teaches the production of amorphous form of another pharmaceutical agent which is also used in the treatment of hypercholesterolemia and hyperlipidemia. See the process steps disclosed in page 4, lines 8-14, wherein the crystalline form is dissolved in a non-hydroxylic solvent, followed by the addition of a non-polar hydrocarbon anti-solvent. In view of the teachings of Kumar (WO'116), one of ordinary skill in the art would have been motivated to prepare the amorphous form of the instantly claimed compound with the reasonable expectation of obtaining result consistent with that of the prior art. Such modification would have been obvious because the skilled artisan would have reasonably expected the prior art synthesis steps to result in the corresponding amorphous form as taught in the prior art.

Duplicate Claims

1. Applicant is advised that should claim 1 be found allowable, claim 7 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

2. Applicant is advised that should claim 8 be found allowable, claim 11 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

3. Applicant is advised that should claim 18 be found allowable, claim 21 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

4. Applicant is advised that should claim 28 be found allowable, claim 31 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claims 7, 11, 21, and 31 are substantial duplicates of claims 1, 8, 18 and 28 respectively and do not further limit the base claims.

Receipt is acknowledged of the Information Disclosure Statement filed on March 17, 2004 and a copy is enclosed herewith.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Tuesday-Friday from 6:30am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Deepak Rao
Primary Examiner
Art Unit 1624

September 20, 2006